Interferon gamma release assay in the diagnosis of tuberculous mastitis

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ABSTRACT

Tuberculous mastitis is rare, especially in Western countries. We describe a case where the interferon gamma release assay blood test led to diagnosis and successful treatment of the disease.

KEYWORDS

Breast – Tuberculosis – Diagnosis

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Tuberculous mastitis is rare, accounting for less than 0.1% of breast biopsies in Western countries.¹ It is usually found in women from countries with a high incidence of tuberculosis. The diagnosis of tuberculous mastitis may be difficult; histology is important² but staining for acid fast bacilli and mycobacterial cultures is commonly negative.

Interferon gamma release assays (IGRAs) are a well established alternative to tuberculin skin testing. IGRA detects the presence of T cells sensitised to antigens specific for *Mycobacterium tuberculosis* (ESAT-6, CFP-10 and TB7.7); positive IGRA indicates latent or active tuberculosis. IGRA is more specific than skin testing and, unlike the skin test, does not cross-react with a previous bacillus Calmette–Guérin vaccination. However, there are few reports of the use of IGRA in the diagnosis of tuberculous mastitis.^{3,4}

Case History

A 35-year-old Spanish woman presented with a 1-month history of a mass in the left breast. She had suffered from recurrent mastitis since the birth of her first child ten months previously. Examination revealed an ill defined lump, with no notable ultrasonography findings. She re-presented two months later with a swollen, erythematous and distorted breast with a 5cm tender lump. Her symptoms had failed to respond to multiple courses of antibiotics. Ultrasonography demonstrated a suspicious indeterminate mass in the left breast, with interlobular fluid and echo-poor regions, thickened skin and one abnormal axillary node. On mammography, the left breast was shrunken and dense, with no masses or calcifications.

Fine needle aspiration (FNA) revealed granulomas consisting of epithelioid cells and mononuclear cells, with a

background of neutrophils and foamy macrophages. Widespread core biopsies revealed diffuse chronic inflammation with foci of microabscesses, granulation tissue and occasional granulomas. Special stains, including Ziehl–Neelsen staining, were negative. Pus swabs failed to grow organisms and were negative for mycobacteria on culture. Gadolinium enhanced magnetic resonance imaging was reported as consistent with a carcinoma, with confluent nodular enhancement, enlarged axillary lymph nodes and thickened skin. These results led to considerable patient anxiety.

The patient was referred for a second opinion and, putting the whole picture together, a diagnosis was made of idiopathic granulomatous mastitis. However, in view of the clinical uncertainty and despite repeated negative cultures of pus aspirated under ultrasonography control, she was referred to the respiratory team to exclude tuberculosis. Suspicion for tuberculosis was low: she had been born in Spain, moving to the UK nine years ago, and she denied weight loss and night sweats. There were no known tuberculosis contacts and her chest x-ray was normal.

However, IGRA (using QuantiFERON®-TB; Cellestis, Cheshire, VIC, Australia) was positive, indicating either latent or active tuberculosis infection. By this stage, the patient's condition was worsening, with multiple fistulas, scarring and distortion of her left breast (Fig 1). Owing to the deteriorating clinical picture and the positive IGRA, she was started on a therapeutic trial of standard antitubercular therapy (rifampicin, isoniazid and pyrazinamide, plus ethambutol). There was a dramatic resolution of breast lesions within eight weeks, and within three months of treatment, the breast looked and felt normal, apart from superficial scarring.

The dramatic response to antitubercular therapy in a patient with granulomatous breast disease is strongly

Figure 1 Appearance before antitubercular therapy

suggestive of tuberculous mastitis. She has required no other treatment, and remains fit and well one year follow-up treatment.

Discussion

This case represents a challenging diagnosis of tuberculous mastitis. There were no obvious risk factors, histopathology was not sufficient for diagnosis, and both staining and culture were negative. The IGRA blood test gave sufficient confidence to start a therapeutic trial of antitubercular triple therapy, which was rapidly successful.

In this case, histopathology was not sufficient for diagnosis and the cultures were negative although a negative culture does not exclude tuberculous mastitis.² Reports suggest that FNA is diagnostic in 70–100% of cases of tuberculous mastitis.² However, its ability to distinguish tuberculous mastitis from other granulomatous diseases is controversial. A study from 2012 found that FNA was diagnostic only in 25% of idiopathic granulomatous mastitis cases and 16.6% of tuberculous mastitis cases.⁵ The positive IGRA result gave confidence

to commence a therapeutic trial of antitubercular treatment. This was critical for a woman who had suffered the trauma of multiple recurring abscesses and imaging suggestive of malignancy, and for whom the clinical condition would have deteriorated while waiting for further culture results, which were repeatedly negative in this case.

Conclusions

A positive IGRA cannot distinguish between active and latent tuberculosis, and therefore must not be used in isolation as a diagnostic test for active disease. However, a positive IGRA may aid the diagnosis of active disease in countries with a lower incidence of latent tuberculosis, such as the UK. There have been few case reports on the use of IGRA in the diagnosis of tuberculous mastitis.^{5,4} This case illustrates how a positive IGRA may give clinicians the confidence to make the diagnosis of tuberculous mastitis in low risk populations when standard investigations are equivocal.

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